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A Novel Electrocardiographic Index to Predict the Severity of Coronary Calcification

ABSTRACT

Objective: Electrocardiogram (ECG) remains an essential tool in cardiology. Coronary artery calcium (CAC) score, measured via computed tomography, is a well-established predictor of cardiovascular risk. However, its cost and availability limit widespread use. This study introduces a novel ECG-based index, the PARLA (Prediction of Ischemia via Angle of QRS-T and corrected QT Length Assessment) Index, combining the QTc interval and frontal QRS-T (fQRS-T) angle, to assess its association with CAC severity.

Methods: This retrospective, cross-sectional study included patients who underwent ECG and coronary computed tomography angiography. Exclusion criteria encompassed conduction abnormalities, significant valvular disease, cardiomyopathy, prior coronary interventions, and medications affecting ECG parameters. The PARLA Index was defined as the sum of the QTc interval and absolute fQRS-T angle. Patients were classified based on CAC score: <100 (low CAC score) vs. ≥100 (high CAC score). Statistical analyses, including logistic regression and receiver operating characteristic (ROC) curve analysis, assessed the predictive value of the PARLA Index for CAC severity.

Results: Among 595 patients (mean age 53.4 ± 11.6 years, 39.5% female), the high-CAC group had older age, higher prevalence of hypertension and diabetes, and greater left ventricular wall thickness. The PARLA Index was significantly higher in the high-CAC group (440 ± 26 vs. 465 ± 37, $P < .001$). Multivariate regression identified the PARLA Index as an independent predictor of CAC ≥100 (OR: 1.021, $P < .001$). ROC analysis determined an optimal PARLA Index cut-off of 450 (AUC: 0.705, sensitivity: 63%, specificity: 66%).

Conclusions: The PARLA Index is a novel, simple ECG-derived parameter that correlates with CAC severity and may serve as a noninvasive tool for cardiovascular risk stratification. Future studies should validate its prognostic value.

Keywords: Coronary artery calcium score, electrocardiogram, PARLA index, QRS-T angle, QTc interval

INTRODUCTION

Electrocardiogram (ECG) remains one of the most widely used diagnostic tools in cardiology, providing crucial insights into the heart's electrical activity. Over the years, numerous indices derived from ECG have been proposed to assist in detecting various cardiac conditions.[1-3] New indices are continuously being developed to improve diagnostic accuracy and prognostic value. The frontal QRS-T angle (fQRS-T) is a novel ECG-derived parameter that reflects the spatial dispersion between ventricular depolarization and repolarization vectors. Recent studies have demonstrated its potential value in cardiovascular risk assessment, severity of coronary artery disease (CAD), complexity of coronary lesions, and coronary atherosclerotic burden.[4-6] These findings support the use of the fQRS-T angle as a noninvasive marker of CAD severity. In addition to the QRS-T angle, the corrected QT interval (QTc) is another widely studied ECG parameter that reflects temporal heterogeneity of ventricular repolarization. The QTc prolongation has been associated with myocardial ischemia, angiographic severity of ischemic heart disease, and adverse cardiovascular outcomes.[7] These findings highlight the potential of the QTc interval and fQRS-T angle as noninvasive markers of ischemic burden, further justifying their inclusion in a composite index for assessing CAD severity.

ORIGINAL INVESTIGATION

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In the last decade, coronary artery calcium (CAC) score has gained attention in cardiovascular risk assessment. The CAC score, obtained through computed tomography (CT), quantifies the burden of calcified plaque in the coronary arteries and is a strong predictor of future cardiovascular events. Recent 2024 ESC Guidelines on Chronic Coronary Syndromes recommend CAC scoring (CACS) in patients with low- to moderate- pre-test probability (5%-50%) of obstructive CAD, to improve risk stratification and guide further diagnostic steps, such as coronary CT angiography (CCTA). This recommendation holds a Class I, level of evidence A rating when used to determine which individuals may safely defer more complex testing.[8] However, despite its prognostic significance, its cost and availability limit the widespread use of the CAC score.

Given the need for simpler, more accessible markers for cardiovascular risk, the present study investigates the relationship between a newly defined ECG index, derived from the sum of the QTc interval and the fQRS-T angle, and the CAC score. This new index combines 2 well-known ECG parameters: the QTc interval, which reflects ventricular repolarization, and the QRS-T angle, which represents the spatial difference between depolarization and repolarization vectors. These 2 ECG markers reflect different but complementary aspects of cardiac repolarization and spatial heterogeneity, which are both known to be associated with coronary atherosclerosis. These parameters have individually been linked to adverse cardiac outcomes, but their combined value in predicting coronary calcification remains unclear.[9-12] This study aims to determine whether this novel ECG index can be a surrogate marker for coronary calcification, providing a noninvasive, cost-effective tool for cardiovascular risk stratification.

METHODS

This study was conducted in a single-centered, retrospective, and cross-sectional design. Between April 2023 and April 2024, 595 patients who were admitted to the Cardiology Clinic of Ankara Bilkent City Hospital and underwent ECG and CCTA based on clinical indication were included in the study. Patients were referred due to suspected stable CAD based on clinical assessment and/or noninvasive tests. These included atypical chest pain, borderline stress test results, low or intermediate pre-test probability for CAD.

Inclusion criteria were:

- Age ≥ 18 years,
- Availability of both resting 12-lead ECG and CCTA,
- Indication for CCTA based on suspected stable CAD.

Exclusion criteria were:

- Complete or incomplete bundle branch block,
- Atrial fibrillation,
- Presence of pathological Q waves on ECG,
- Known cardiomyopathy or moderate to severe valvular heart disease,
- History of myocardial infarction, percutaneous coronary intervention, or coronary artery bypass grafting,
- Poor ECG quality that prevented accurate measurement,
- Use of medications known to affect ventricular depolarization or repolarization (e.g., antiarrhythmics, antipsychotics, antidepressants),
- Electrolyte abnormalities at the time of ECG.

The clinical and demographic characteristics of the patients, risk factors, echocardiographic left ventricular ejection fractions, left ventricular end-diastolic diameters, left ventricular wall thicknesses, CAC scores, ECG parameters, and various hematological and biochemical parameters from blood samples were recorded. Hypertension was defined as having a systolic blood pressure of ≥140 mm Hg and/or a diastolic blood pressure of ≥90 mm Hg in at least 2 separate measurements, or the ongoing use of any antihypertensive medication. Diabetes mellitus (DM) was defined as a fasting plasma glucose level exceeding 126 mg/dL, a glucose level greater than 200 mg/dL at any measurement, or the active use of an antidiabetic medication. The medical records of the patients were retrospectively analyzed. The CAC was detected using a 512-row multi-detector CT scanner (Revolution; GE Healthcare, Milwaukee, WI, USA) and quantified using the Agatston method. As several guidelines consider a CAC score ≥100 as a threshold for initiating aspirin and statin therapy and for reclassifying risk groups, patients were divided into 2 groups based on their CAC scores (<100 and ≥100), and analyses were conducted accordingly.[13,14]

Twelve lead ECGs were recorded in the supine position during outpatient visits using a standard ECG device (MAC 2000, GE Medical Systems Information Technologies, Wisconsin, USA) at a speed of 25 mm/s and a voltage of 10 mm/mV. All ECGs were obtained prior to the administration of any beta-blockers used for CT preparation. Therefore, ECG parameters were not influenced by beta-blocker administration. The recordings were retrospectively reviewed from hospital digital record archives. Heart rate, QRS duration, QT duration, QTc duration, PR duration, QRS angle, P angle, and T angle were transcribed from the computer interpretation of the ECG. Two cardiologists verified the measurements. This was accomplished by integrating 4-fold magnified digital ECG images with DFR Calipers (a software program developed by A.J. Rogers, Stanford University, CA, USA). The ECG records that were not satisfactory for signal quality were excluded. The QT interval was measured from the beginning of the QRS complex to the end of the T wave and adjusted for heart rate using the Bazett formula: $QTC = QT\sqrt{(R\text{-}R\ interval)}$. Frontal QRS axis and T axis were obtained from the automatic report section of the ECG device. These angles were checked. Frontal QRS-T angle was

HIGHLIGHTS

- A novel electrocardiogram index combining QTc interval and frontal QRS-T angle was introduced.
- The index showed a correlation with coronary artery calcium scores.
- It may serve as a noninvasive predictor of atherosclerosis.
- The findings support its potential role in early cardiovascular risk assessment.

defined as the absolute difference between the QRS axis and the T axis (frontal QRS-T angle = |QRS axis – T axis|). If this angle exceeded 180°, the current angle was subtracted from 360° and recalculated.[15]

A novel index was described using electrocardiographic QRS-T Angle and QTc duration (Prediction of Ischemia via Angle of QRS-T and corrected QT Length Assessment: PARLA index). The PARLA index was calculated by summing the fQRS-T angle absolute value and QTc duration in ms: PARLA Index = QTc (ms) + frontal QRS-T angle (Figure 1).

The study was conducted under the principles stated in the Helsinki Declaration and was approved by the Local Ethics Committee (Ethics committee no 2-24-150, April 17, 2024). Informed consent was waived since the record based retrospective design.

Statistical Analysis

Statistical analyses were performed using the SPSS 18 Statistical Package Program for Windows (SPSS Inc., Chicago, IL, USA). The normality of data distribution was assessed using the Kolmogorov–Smirnov test, while variance homogeneity across groups was evaluated with Levene's test. Descriptive data were presented as percentage frequencies for categorical variables. Quantitative variables following a normal distribution were expressed as mean ± standard deviation, whereas those with a non-normal distribution were reported as median (25^{th} percentile-75^{th} percentile). Group comparisons for categorical variables were conducted using the chi-square test. Student's *t*-test was applied for continuous variables to compare normally distributed data between independent groups, while the Mann–Whitney *U*-test was used for non-normally distributed data. Binary logistic regression analysis was performed to determine the odds ratios (ORs) and 95% CIs of potential predictors for a CAC score ≥100. The cut-off values of the fQRS-T angle, QTc duration, and PARLA Index for predicting a CAC score ≥100 were determined using receiver operating characteristic (ROC) curve analysis. A *P*-value of <.05 was considered statistically significant.

RESULTS

Based on CAC scores, 595 patients were divided into 2 groups. Group 1 consisted of 365 patients with a CAC score of

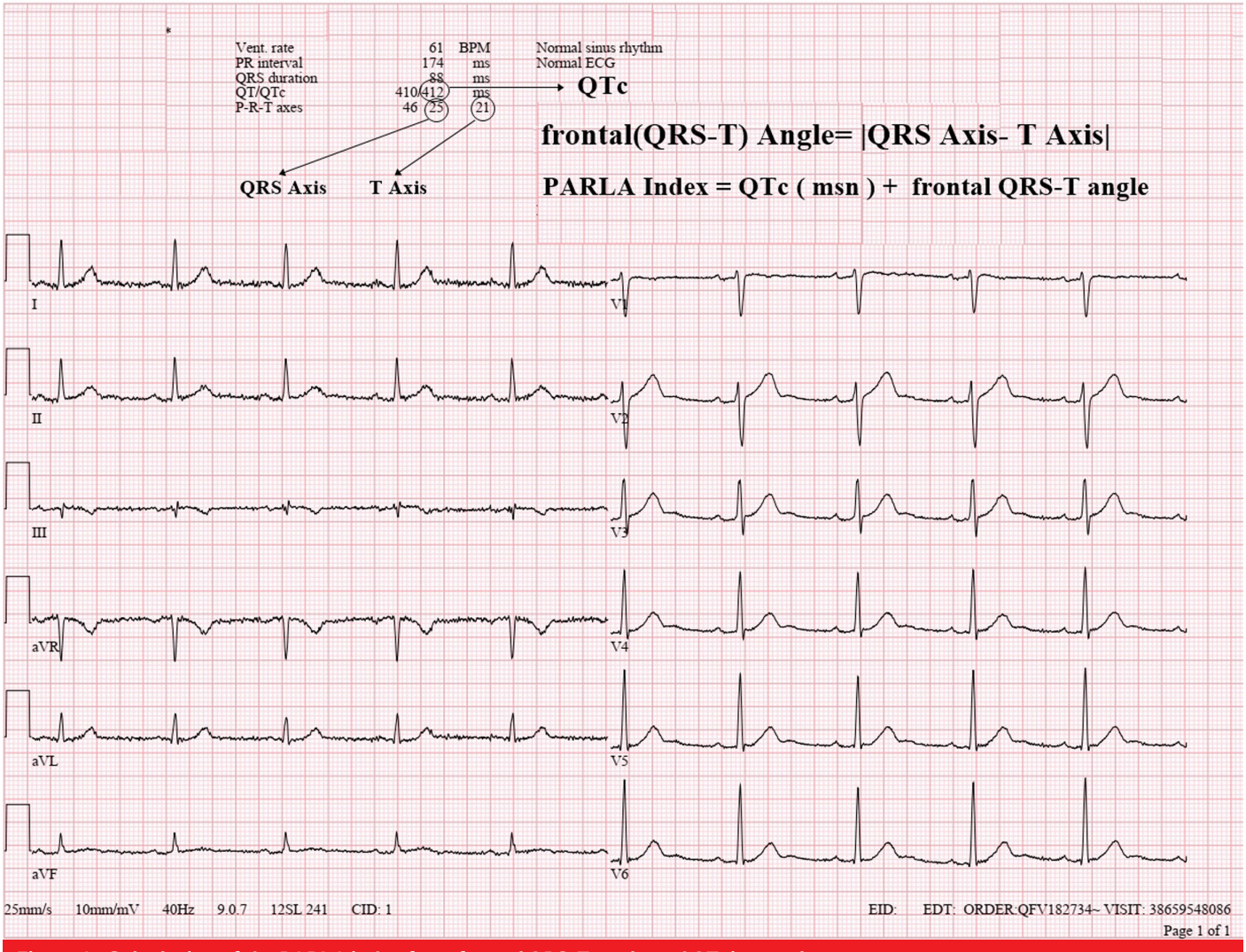

Figure 1. Calculation of the PARLA index from frontal QRS-T angle and QTc interval.

<100, while group 2 included 230 patients with a CAC score of ≥100. Among the 595 patients, 235 (39.5%) were female. The mean age of the study population was 53.4 ± 11.6 years. Baseline demographic characteristics, laboratory results, and transthoracic echocardiographic findings are summarized in Table 1. The CAC score ≥100 group consisted of older patients (49 ± 10 years vs. 61 ± 9 years; $P < .001$) and frequencies of DM and hypertension were also higher in this group ($P < .001$). Frequency of males was significantly higher in the CAC score ≥100 group ($P = .001$) and smokers were similar in both groups ($P = .423$).

Blood glucose and creatinine levels were significantly higher in the CAC score ≥100 group ($P < .001$ and $P = .033$ respectively). Additionally, potassium levels were slightly lower in the CAC score ≥100 group ($P = .045$) and total cholesterol, low density lipoprotein cholesterol, and high density lipoprotein cholesterol were similar in both groups.

In echocardiographic parameters, left ventricle ejection fractions and left ventricle end-diastolic diameters were similar in both groups ($P = .082$ and $P = .596$, respectively), while left ventricle wall thicknesses were higher in the CAC score ≥100 group ($P > .001$).

The electrocardiographic parameters, heart rate, QRS duration, T angle, and P angle showed no significant differences between the 2 groups ($P = .674$; $P = .367$; $P = .426$ and $P = .813$ respectively). In contrast, significant differences were observed between the 2 groups in QRS duration, QT

Table 1. Demographic, Clinical, and Laboratory Characteristics of the Study Population According to Coronary Calcification Score Groups

	CAC Score < 100 n = 365	CAC Score ≥ 100 n = 230	*P*
Age, years	49 ± 10	61 ± 9	<.001
Sex, female, (%)	164 (44.9)	71 (30.9)	.001
Smokers, (%)	145 (39.7)	99 (43.0)	.423
Diabetes mellitus, (%)	48 (13.2)	71 (30.9)	<.001
Hypertension, (%)	102 (27.9)	128 (55.7)	<.001
Glucose, mg/dL	91 (85-99)	95 (85-118)	<.001
Creatinine, mg/dL	0.82 ± 0.16	0.85 ± 0.16	.033
Sodium, mEq/L	140 ± 2	140 ± 2	.208
Potassium, mEq/L	4.40 ± 0.35	4.33 ± 0.35	.045
Total cholesterol, mg/dL	202 ± 42	201 ± 55	.737
Triglyceride, mg/dL	145 (101-201)	160 (109-210)	.429
High density lipoprotein, mg/dL	44 (36-52)	42 (37-50)	.435
Low density lipoprotein, mg/dL	122 (99-143)	118 (95-145)	.669
Leukocytes, /mm^3	7.400 ± 1.903	7.548 ± 1.852	.362
Hemoglobin, g/dL	14.3 ± 1.6	14.3 ± 1.6	.847
Platelets, /mm^3	259.244 ± 63.196	253.653 ± 61.490	.299
Echocardiography			
Left ventricular ejection fraction, %	60 ± 4	59 ± 4	.082
End-diastolic diameter, mm	46 ± 3	46 ± 3	.596
Interventricular septum thickness, mm	10 ± 1.4	11.2 ± 1.6	<.001
Left ventricle posterior wall thickness, mm	9.6 ± 1.2	10.3 ± 1.2	<.001
Electrocardiography			
Heart rate, bpm	76 ± 12	76 ± 13	.674
QRS duration	84 ± 10	85 ± 10	.367
QT duration	373 ± 27	384 ±32	<.001
QTc duration	416 ± 20	426 ± 25	<.001
PR duration	145 ± 19	150 ± 20	<.001
QRS angle	34 (12-58)	12 (–13 to 37)	<.001
P angle	53 ± 20	53 ± 20	.813
T angle	43 (27-57)	44 (27-57)	.426
QRS-T angle	19 (10-33)	32 (18-57)	<.001
PARLA index	440 ± 26	465 ± 37	<.001
Coronary calcium			
Agatstone score	0 (0-2)	284 (171-496)	

duration, QTc duration, PR duration, and QRS angle ($P < .001$). The PARLA index was also significantly higher in the CAC score ≥100 group (440 ± 26 vs. 465 ± 37; $P < .001$).

In univariate regression analysis, age, male sex, DM, hypertension, glucose, creatinine, potassium, left ventricular ejection fraction, interventricular septum thickness, and PARLA index were associated with a CAC score ≥ 100. In multivariate logistic regression analyses model including age, DM status, hypertension, creatinine, potassium, left ventricle ejection fraction, and interventricular septum thickness, the PARLA index was an independent predictor of CAC score ≥ 100 [OR: 1.021; 95% CI: (1.012-1.030); $P > .001$], see Table 2.

According to ROC curve analysis, the best cut-off value of the PARLA index for predicting the CAC score ≥100 was 450 with a 63% sensitivity and 66% specificity (AUC: 0.705; 95% CI: 0.661-0.748; $P < .001$), see Figure 2. The PARLA index had a higher area under the curve than QRS-T angle (AUC: 0.661; 95% CI: 0.615-0.707; $P < .001$) and QTc duration (AUC: 0.606; 95% CI: 0.559-0.653; $P < .001$) for predicting the CAC score ≥100.

DISCUSSION

This study introduced a new ECG index for predicting coronary artery calcification. The PARLA index, the sum of the fQRS-T angle and QTc duration, was independently associated with coronary artery calcification and a higher yield in stratifying patients compared to the individual QRS-T angle and QTc duration. Regarding the significance of markers in predicting risk for patients with chronic coronary syndrome, the results might contribute to expanding the cardiovascular management tool inventory.

Coronary artery calcium scanning has been recommended for risk stratification to identify individuals who may benefit from intensified primary prevention. In chest pain cases, assessing the calcium score increases the likelihood of identifying obstructive CAD. Longitudinal studies indicate that Agatston scores exceeding 100 are associated with an increased risk of cardiac events, supporting enhanced preventive measures such as statin and low-dose aspirin therapy.[16,17] In this context, the development of markers that can predict CAC scores would be beneficial for the risk stratification of this patient group. Surface ECG remains a valuable tool for demonstrating the heart's electrical activity. Although ST and T segment changes in ECG are more commonly used for detecting ischemia, various parameters such as the QRS-T angle and QTc interval are practical in predicting cardiovascular risk in different patient populations.[18-20]

Several studies have previously demonstrated the clinical relevance of both the fQRS-T angle and the QTc in the context of CAD. A wider fQRS-T angle has been associated with increased coronary atherosclerotic burden, higher SYNTAX scores, and adverse cardiovascular outcomes, even in stable CAD populations.[4-6] Similarly, QTc prolongation has been shown to correlate with the severity of myocardial ischemia, including in low- to intermediate-risk patients presenting with chest pain.[21] Earlier angiographic studies also reported a gradual increase in QTc duration with the extent of ischemic heart disease.[7] These findings collectively support the prognostic value of both ECG-derived parameters, reinforcing

Table 2. Binary Logistic Regression Analysis for Coronary Calcium Score Groups

	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Age, years	1.144 (1.117-1.171)	<.001	1.152 (1.115-1.189)	<.001
Sex, female	1.825 (1.289-2.585)	.001	3.740 (1.827-7.658)	<.001
Smokers	1.136 (0.8131.588)	.455		
Diabetes mellitus	2.930 (1.939-4.428)	<.001	1.197 (0.617-2.323)	.595
Hypertension, (%)	3.255 (2.301-4.605)	<.001	1.860 (1.068-3.241)	.028
Glucose, mg/dL	1.011 (1.006-1.017)	<.001		
Creatinine, mg/dL	3.945 (1.421-10.954)	.008	0.253 (0.040-1.597)	.144
Sodium	1.052 (0.970-1.140)	.222		
Potassium	0.610 (0.373-0.998)	.049	0.770 (0.341-1.741)	.530
Total cholesterol, mg/dL	1.000 (0.996-1.003)	.869		
Triglyceride, mg/dL	1.000 (0.998-1.001)	.874		
High density lipoprotein, mg/dL	0.991 (0.978-1.004)	.181		
Low density lipoprotein, mg/dL	1.000 (0.996-1.005)	.816		
Leukocytes, /mm^3	1.037 (0.949-1.133)	.427		
Hemoglobin, g/dL	0.994 (0.894-1.105)	.905		
Platelets, /mm^3	0.999 (0.996-1.001)	.296		
Left ventricular ejection fraction, %	0.929 (0.888-0.972)	.001	1.008 (0.943-1.077)	.811
End-diastolic diameter, mm	1.550 (0.921-2.609)	.099		
Interventricular septum thickness, mm	1.519 (1.313-1.757)	<.001	1.121 (0.939-1.339)	.206
PARLA index	1.026 (1.020-1.033)	<.001	1.021 (1.012-1.030)	<.001

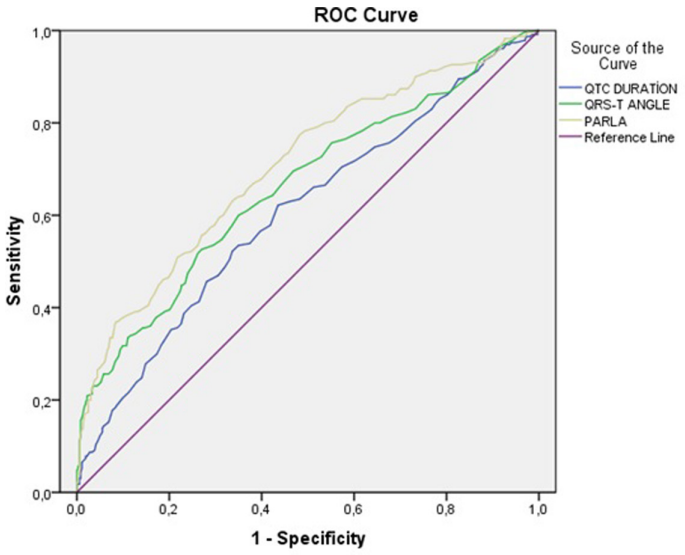

Figure 2. Receiver operating characteristic curve of PARLA index for predicting of high coronary artery calcium (Agatston score ≥100).

their inclusion in composite indices such as the PARLA Index for estimating CAD severity.

Normally, the balanced regulation of electrical activity and recovery ensures that the ventricular depolarization and repolarization axes are aligned in the same direction. Chronic ischemic myocardium causes conduction delays in local Purkinje fibers and partial depolarization and repolarization of the ventricle, leading to slow myocardial activation. This slow activation is one of the primary causes of depolarization and repolarization heterogeneity. As a result, ischemia-induced damaged or heterogeneous myocardial regions lead to abnormal ventricular repolarization and an increased QRS-T angle. In a study conducted on patients with FFR-proven ischemia, the fQRS-T angle was found to be wider.[22] Likewise, in this study, the QRS-T angle was wider in the high CAC score group. However, unlike ischemia demonstrated by physiological studies, the CAC score is an indicator of the global atherosclerotic burden. Therefore, the pathophysiological link between coronary atherosclerosis and the QRS-T angle needs to be elucidated.[23]

The QTc interval is a measure that reflects ventricular repolarization, and a prolonged QTc interval predisposes individuals to ventricular arrhythmias and sudden cardiac death.[24] On the other hand, ischemia itself also contributes to the prolongation of the QT interval. In the presence of transmural ischemia, QTc interval prolongation has been observed in all patients.[25] In a study conducted on patients with acute chest pain, the QTc interval on the hospital admission ECG correlated with the underlying myocardial ischemia.[21] Likewise, in a study, Cho et al[26] investigated the predictive value of QT prolongation in assessing obstructive CAD among patients presenting with suspected angina. The study demonstrated that the QTc interval is associated with the presence and severity of obstructive CAD and revealed that a new risk score model incorporating the QTc interval offers a higher predictive power for detecting obstructive CAD compared to the traditional risk scores. Additionally, studies showed that the QTc interval is also prolonged in subclinical atherosclerotic cardiovascular diseases and manifested atherosclerotic cardiovascular disease as well.[20,27] Similar to the results of the study, previous studies have also found an association between coronary calcium score and QTc interval.[23,28] The potential use of the combination of QRS-T angle and QTc interval in predicting the CAC score severity was investigated.

Beyond the fQRS-T angle and QTc interval, other ECG-derived indices have also emerged as valuable tools in cardiovascular risk stratification. For instance, the MVP ECG Risk Score has been shown to predict long-term atrial fibrillation in patients with implantable cardioverter-defibrillators and heart failure with reduced ejection fraction.[29] Likewise, the Electrocardiographic Diastolic Index—a simple ECG-based formula—has been associated with echocardiographic parameters of diastolic dysfunction.[30] These novel approaches highlight a growing interest in leveraging surface ECG data for noninvasive risk prediction across a spectrum of cardiovascular conditions. The PARLA Index aligns with this trend by proposing a composite ECG-based parameter aimed at identifying individuals with more severe coronary calcification.

The newly established PARLA index was defined as the sum of the fQRS-T angle and QTc values. The relationship between the fQRS-T angle and QTc with myocardial ischemia, their predictive value in the incidence of CAD, and their prognostic role in predicting short- and long-term cardiovascular events have been investigated and emphasized over the past several decades. While individual ECG markers such as QTc interval and QRS-T angle have been associated with cardiovascular outcomes, their combined utility for predicting subclinical coronary calcification has not been established. Based on this information, the PARLA index was defined, which is expected to better predict the atherosclerotic burden. Compared to its components, the PARLA index demonstrated better predictive performance in identifying patients with higher CAC scores. Besides, the PARLA index predicted the severity of the CAC score independently of parameters such as age, gender, and diabetes, which could potentially affect the QTc interval and QRS-T angle. The underlying mechanism linking the PARLA Index to CAC severity may involve ischemia-induced repolarization abnormalities, autonomic dysfunction, and myocardial fibrosis. Future studies using cardiac magnetic resonance imaging or perfusion imaging could further elucidate this relationship.

Study Limitations

This study has several limitations. Being a retrospective, observational, and single-center study, it cannot establish causality as it was conducted in a referral hospital where patients likely had a higher baseline cardiovascular risk. This limits the generalizability of the findings to lower-risk or asymptomatic populations. Additionally, while the PARLA Index was associated with CAC severity, the study did not assess its relationship with ischemia or major adverse

cardiovascular events, which would be important for determining its true clinical relevance. Another limitation is the potential influence of electrolyte levels, particularly magnesium and calcium, which were not fully accounted for but could impact QTc duration and QRS-T angle. Lastly, the findings need validation in larger, prospective, multicenter studies to confirm the PARLA Index's utility in cardiovascular risk stratification.

CONCLUSIONS

The PARLA index is a relatively simple method, and QRS-T angle and QTc interval are supplied automatically by most of the ECG machines. This simple ECG index may facilitate the identification and stratification of patients with suspicion of atherosclerosis. Therefore, future studies may explore the potential of the PARLA index as a marker in the management of atherosclerosis and ischemia.

Statement on the Use of Artificial Intelligence: Artificial intelligence was not used in the preparation of the article.

Ethics Committee Approval: This study was approved by the Ankara Bilkent City Hospital Institutional Ethics Committee (No: 2-24-150, dated April 17, 2024) and respected the principles outlined in the Declaration of Helsinki.

Informed Consent: Informed consents were waived since the record based retrospective design.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – S.D.; Design – S.D.; Data Collection or Processing – K.A., R.C.K., A.A.; Analysis or Interpretation – S.D., M.D., P.T.D.; Literature Search – S.D., M.D., P.T.D.; Writing – S.D.; Approval – P.T.D.

Declaration of Interests: The authors have no conflicts of interest to declare.

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